

REMARKS

I. Introduction

Receipt of a non-final Office Action dated June 20, 2006, is acknowledged. In the Action, claims 1-14 are rejected as allegedly obvious over Wiedmann *et al.*, U.S. Patent No. 5,747,001 (“Wiedmann”), in view of Tabibi *et al.*, U.S. Patent No. 6,682,758 (“Tabibi”), Osbakken *et al.*, U.S. Patent Application Publication 2002/0061281 (“Osbakken”), or Saidi *et al.*, U.S. Patent No. 6,241,969 (“Saidi”).

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

II. Status of the Claims

In this response, no claims were cancelled or amended, and no new claims were added. Therefore, claims 1-14 are under examination.

III. Rejection of the Claims Under 35 U.S.C. § 103

A. *Wiedmann in view of Tabibi*

Claims 1-14 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Wiedmann, in view of Tabibi. Specifically, the claims are rejected because “[i]t would have been obvious . . . to have implemented the sterile filtration [*sic*] as taught by Tabibi in the formulations and process of Wiedmann, since Wiedmann teaches filtration [*sic*] of nanoparticles of beclomethasone and tyloxapol.” Office Action at 3. The Office further states that “one of ordinary skill in the art would have been motivated to implement sterile filtration [*sic*] of Tabibi instead of simple filtration [*sic*] of Wiedmann because sterilization of formulations is beneficial to recipients. Applicants respectfully traverse this ground for rejection.

To establish a *prima facie* case of obviousness, there must be: (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) when combined, a teaching or suggestion of all the claim

limitations in the prior art references. *See* MPEP §2143 (Aug. 2001). “Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).

As the Office concedes, Wiedmann does not teach sterile filtered nanoparticulate active agent formulations, as required by the claimed invention. Specifically, the claimed invention recites a composition comprising nanoparticulate beclomethasone particles, nanoparticulate budesonide particles, or a combination thereof, having tyloxapol as a surface modifier, and having an effective particle size of less than about 150 nm, wherein the nanoparticulate composition is sterile filtered. *See, e.g.* Claim 1. Under U.S. Patent Laws, however, the teachings in Wiedmann cannot be combined with Tabibi.

As noted in the application, Applicants surprisingly discovered that only tyloxapol would function to stabilize budesonide and beclomethasone at a small enough particle size to be sterile filtered. Moreover, unexpectedly, this small particle size was not obtained using tyloxapol as a surface modifier for other corticosteroids. Nothing within Wiedmann or Tabibi points the skilled artisan to the unexpected combination discovered by applicants – beclomethasone or budesonide in combination with tyloxapol – which results in compositions having small enough particle sizes to enable sterile filtration. Prior to the present invention, it was not known that this particular combination of drug and surface modifier could even be sterile filtered.

In particular, Tabibi describes a drug delivery system for water-insoluble compounds comprising a water-insoluble drug, a water-miscible organic solvent, a surfactant, and water. Tabibi, however, only states that the *surfactant* preferably form vesicles having a size of about 50-200 nm and therefore, does not describe a nanoparticulate *drug* or sterile filtering such a drug. Although Tabibi does mention sterile filtration, the motivation to combine Tabibi with Wiedmann is simply not present in cited art.

Therefore, while the Office refers to sterile formulations in general as “beneficial to recipients” and uses this as a basis for combining the cited references (Office Action at 3), there is no specific teaching in the cited references that would lead one of skill in the art to

identify a particular drug/surface modifier combination and sterile filter this formulation with a reasonable expectation of success. After all, neither beclomethasone or budesonide *not* having tyloxapol as a surface modifier, nor other corticosteroids having tyloxapol as a surface modifier, can be sterile filtered. Accordingly, this is at best “obvious to try” sterile filtering a nanoparticulate beclomethasone or budesonide and tyloxapol combination, which has long been held to not constitute obviousness. *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210 (Fed. Cir. 1995).

Therefore, for at least these reasons, Applicant respectfully request that the rejection be withdrawn.

B. *Wiedmann in view of Osbakken*

Claims 1-14 are rejected under 35 U.S.C. § 103 as allegedly obvious over Wiedmann, in view of Osbakken. In particular, the claims are rejected because “[i]t would have been obvious . . . to have implemented the sterile filtration [*sic*] as taught by Osbakken in the formulations and process of Wiedmann, since Wiedmann teaches filtration [*sic*] of nanoparticles of beclomethasone and tyloxapol.” Office Action at 3. The Office further states that “one of ordinary skill in the art would have been motivated to implement sterile filtration [*sic*] of Osbakken instead of simple filtration [*sic*] of Wiedmann because sterilization of formulations is beneficial to recipients. Applicants respectfully traverse this ground for rejection.

As stated above, Wiedmann does not describe sterile filtering nanoparticulate beclomethasone or budesonide, and tyloxapol, and for similar reasons provided above, Osbakken does not cure this deficiency. Indeed, there is no motivation in Osbakken to modify the teachings of Wiedmann and sterile filter a tyloxapol and budesonide or beclomethasone composition with a reasonable expectation of success. The specific combination of drug and surface modifier was surprisingly identified by Applicants to be suitable for sterile filtration. Simply relying on the formulation as being “beneficial to recipients” does not support a suggestion or motivation to modify the references AND a reasonable expectation of success, as required to establish a *prima facie* case of obviousness.

Therefore, for at least these reasons, Applicant respectfully request that the rejection be withdrawn.

C. *Wiedmann in view of Saidi*

Claims 1-14 are rejected under 35 U.S.C. § 103 as allegedly obvious over Wiedmann, in view of Saidi. In particular, the claims are rejected because “[i]t would have been obvious . . . to have implemented the sterile filtration [*sic*] as taught by Saidi in the formulations and process of Wiedmann, since Wiedmann teaches filtration [*sic*] of nanoparticles of beclomethasone and tyloxapol.” Office Action at 3. The Office further states that “one of ordinary skill in the art would have been motivated to implement sterile filtration [*sic*] of Saidi instead of simple filtration [*sic*] of Wiedmann because sterilization of formulations is beneficial to recipients. Applicants respectfully traverse this ground for rejection.

As stated above, Wiedmann does not describe sterile filtering nanoparticulate beclomethasone or budesonide, and tyloxapol, and for similar reasons provided above, Saidi does not cure this deficiency. Although Saidi describes corticosteroid compositions for nasal and pulmonary delivery, Saidi does not relate to a nanoparticulate drug formulation. In fact, the concept of drug particle size is irrelevant in the Saidi patent because the drug is in solution. Therefore, one of skill in the art would not have been motivated to modify the nanoparticulate composition of Wiedmann, and combine it with Saidi to obtain the claimed sterile filtered nanoparticulate composition since Saidi doesn’t even relate to a nanoparticulate drug.

Therefore, for at least these reasons, Applicant respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and arguments. The present application is now in condition for allowance. Early notice to that effect is earnestly solicited.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date Sept 8, 2006

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